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1 IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: John R. Duchek

Art

Unit: 1625

Serial No.: 10/533,576

Filed: May 3, 2005

Confirmation No.: 2302

For: CANNABINOID CRYSTALLINE DERIVATIVES AND PROCESS OF CANNABINOID
PURIFICATION

Examiner: Bernard I. Dentz

March 13, 2008

Declaration of Inventor John R. Duchek

I, John R. Duchek, declare as follows:

1. I am the sole inventor of the subject matter claimed in the above-entitled United States patent application, Serial Number 10/533,576.
2. I have reviewed the Office action issued December 20, 2007 for this application, as well as the Fahrenholtz patent (U.S. Patent No. 3,636,058) and the Maseda et al. article (*Journal of Forensic Sciences*, 1983) cited therein. I have also reviewed all pending claims of this application, including claims 3-5, 8-15 and 18-21.
3. The present invention is directed to processes that, in relevant part, comprise a step of reacting or esterifying at least one cannabinoid with at least one aryl sulfonyl halide in the presence of at least one base that is a tertiary alkyl amine, and in particular a tertiary lower alkyl amine having the formula $R_5R_6R_7N$

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(where each of R_5 , R_6 and R_7 are lower alkyls of 1 to about 6 carbon atoms), to form a cannabinoid aryl sulfonate.

4. The Maseda et al. reference discloses a reaction between tetrahydrocannabinol or cannabinol with 4-dimethylaminoazobenzene-4'-sulfonyl chloride (i.e., dabsyl chloride) in the presence of sodium carbonate. (See, e.g., page 911, last paragraph and page 912, last paragraph.) Notably, no reference is made to the use of a tertiary lower alkyl amine base, or any amine for that matter, in place of the sodium carbonate.

5. The Fahrenholtz patent discloses a conventional method of purifying cannabinoids. Specifically, Fahrenholtz reacts a mixture of the delta-9-tetrahydrocannabinol and delta-8-tetrahydrocannabinol with *m*-nitrobenzenesulfonyl chloride in the presence of pyridine. (See, e.g., column 14, lines 73.) Notably, no reference is made to the use of a tertiary lower alkyl amine base in place of pyridine.

6. Furthermore, the pyridine base disclose by Fahrenholtz is not readily interchangeable with the tertiary lower alkyl amine base of the presently claimed processes. This is because:

- (a) Pyridine has a pKa of about 5.2, whereas tertiary alkyl amines, and in particular tertiary lower alkyl amines, have a pKa of about 11. These respective pKa values mean that lower tertiary alkyl amines are significantly more

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basic than pyridine. Specifically, tertiary lower alkyl amines are about one million times more basic than pyridine.

- (b) The by-products formed using these bases are tertiary lower alkyl amine hydrochlorides or pyridine hydrochloride. These by-products are acidic. Furthermore, the pyridine hydrochloride is significantly more acidic than the tertiary lower alkyl amine hydrochlorides, about one million times more acidic.
- (c) The presence of the above-noted pyridine hydrochloride in the reaction mixture is undesirable for a number of reasons, including because it is such a strong acid. For example, in the case of tetrahydrocannabinol (THC), the acid results in the conversion of the more desirable delta-9 isomer to the less desirable delta-8 isomer.
- (d) In addition to being much less acidic, the tertiary lower alkyl amine hydrochlorides typically precipitate out of the reaction mixture, making them even less likely to cause unfavorable side-reactions to occur (such as the above-noted conversion of the delta-9-THC to the delta-8-THC isomer).

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7. In view of the foregoing, the Fahrenholtz patent and the Maseda et al. reference do not disclose or suggest a process that, in relevant part, comprises a step of reacting or esterifying at least one cannabinoid with at least one aryl sulfonyl halide in the presence of at least one base that is a tertiary alkyl amine, and in particular a tertiary lower alkyl amine having the formula $R_5R_6R_7N$ (where each of R_5 , R_6 and R_7 are lower alkyls of 1 to about 6 carbon atoms), to form a cannabinoid aryl sulfonate, as required by the pending claims of the present application.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

John R. Duchek, Ph.D.
John R. Duchek Ph.D.

March 14, 2008
Date